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DATE: Tuesday, September 27, 2005

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DB=PGPB,USPT,JPAB,DWPI; PLUR=YES; OP=ADJ

<input type="checkbox"/>	L6	L5 and eye	78
<input type="checkbox"/>	L5	l1 and L4	93
<input type="checkbox"/>	L4	(inhibit\$ or reduc\$ or suppress\$) near3 (neovasculari\$ or angiogen\$)	11921
<input type="checkbox"/>	L3	L2 and eye	99
<input type="checkbox"/>	L2	L1 and (neovasculari\$ or angiogen\$)	140
<input type="checkbox"/>	L1	PEDF	169

END OF SEARCH HISTORY

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=> s PEDF
L1 727 PEDF

=> s (neovascular? or angiogen?) (3a) (inhibit? or suppres? or block?)
L2 24387 (NEOVASCULAR? OR ANGIOGEN?) (3A) (INHIBIT? OR SUPPRES? OR BLOCK?)
)

=> s l1 and l2
L3 260 L1 AND L2

=> s l3 and eye
L4 160 L3 AND EYE

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 100 DUP REM L4 (60 DUPLICATES REMOVED)

=> d bib abs 1-20

L5 ANSWER 1 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:611995 CAPLUS

DN 143:126814

TI Compositions and methods for combined therapy of disease by RNAi compound

reduction of expression of one gene and second compound increasing

expression of second gene

IN Reich, Samuel J.; Tolentino, Michael J.

PA The Trustees of the University of Pennsylvania, USA

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
------------	------	------	-----------------

DATE

PI WO 2005062957 A2 20050714 WO 2004-US43454 20041223

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,

MR, NE, SN, TD, TG

PRAI US 2003-532099P P 20031223

AB A desired physiol. state can be induced by altering the aml. of gene

products in target cells of a subject. The target cells are treated with

at least one compd. designed to reduce expression of at least one first

gene by RNAi, and with at least one compd. designed to increase expression

from at least one second gene. The reduced expression of the first gene

and the increased expression from the second gene in the target cells

induces the desired physiol. state in the subject. By altering target

cell gene expression in this way, conditions such as angiogenesis or tumor

growth and metastasis can be inhibited. The hypoxia-induced increase of

human vascular endothelial growth factor (VEGF) levels in HEK 293 cells

was reduced significantly in cells transfected with plasmids expressing

pigment epithelium-derived factor (***PEDF***) and siRNA targeting

VEGF in a dose-dependent manner.

L5 ANSWER 2 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:405387 CAPLUS

DN 142:442338

TI Use of pigment epithelium-derived factor and its peptides to treat

conditions involving increased vascular permeability or increased angiogenesis

IN Tong, Patrick; Liu, Hua

PA The Johns Hopkins University, USA

SO PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
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DATE

PI WO 2005041887 A2 20050512 WO 2004-US36245
20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY,
BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
FI, GB, GD,
GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE,
SN, TD, TG
PRAI US 2003-515374P P 20031029
AB The present invention relates to method of treating a patient
with a
condition involving increased vascular permeability or increased
angiogenesis comprising administering to the patient a
therapeutically
effective amt. of ***PEDF***, ***PEDF*** 44 AA peptide, a
homolog
of the ***PEDF*** 44 AA peptide, a homolog of the
PEDF 44 AA
peptide wherein amino acid residues glutamate at the (101)
amino acid
position, isoleucine at the (103) amino acid position, leucine at
the
(112) and serine at the (115) amino acid position are unchanged,
or an
agent that activates the ***PEDF*** receptor. Conditions for
treatment include, but are not limited to, sepsis, acute respiratory
distress syndrome, nephrotic syndrome, diabetic neuropathy,
preproliferative diabetic retinopathy, cancer or proliferative
diabetic
retinopathy.

L5 ANSWER 3 OF 100 CAPLUS COPYRIGHT 2005 ACS on
STN
AN 2005:283364 CAPLUS
DN 142:349102
TI Combinations of a VEGF receptor inhibitor with other agents for
therapeutic use
IN Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian;
Kinder,
Frederick Ray; Lane, Heidi; Latour, Elisabeth Jeanne; Manley,
Paul
William; Wood, Jeanette Marjorie
PA Novartis Ag, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE

PI WO 2005027973 A2 20050331 WO 2004-EP10701
20040923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY,
BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
FI, GB, GD,
GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE,
SN, TD, TG
PRAI US 2003-505255P P 20030923
OS MARPAT 142:349102

AB The invention discloses a combination therapy for treating
patients
suffering from diseases characterized by cell proliferation and
infiltration of inflammatory cells, coronary diseases, hypertension,
renal
diseases, diabetes, or ocular diseases and conditions. The
patient is
treated with a combination of a VEGF inhibitor compd. and one
or more
second therapeutic agents selected from angiostatic steroids,
photosensitizers, implants contg. corticosteroids, AT1 receptor
antagonists, ACE inhibitors, cyclooxygenase inhibitors, IGF-IR
inhibitors,
mTOR kinase inhibitors, somatostatin receptor antagonists,
P13K
inhibitors, Raf kinase inhibitors, PKC inhibitors; xiii. integrin
antagonists, endogenous anti-angiogenic mols., and
PEDF (pigment
epithelium-derived factor) and analogs.

L5 ANSWER 4 OF 100 CAPLUS COPYRIGHT 2005 ACS on
STN
AN 2005:141111 CAPLUS
DN 142:234460
TI Protein and nucleotide sequences of human, mouse and rat
PEDF -R
and its therapeutic uses
IN Becerra, Patricia S.; Notari, Luigi; Laborda, Jorge; Martinez,
Julio
Escribano
PA The Government of the United States of America, as
Represented by the
Secretary Department of Health and Human Services, USA
SO PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE

PI WO 2005014645 A2 20050217 WO 2004-US25560
20040805
WO 2005014645 A3 20050616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY,
BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
FI, GB, GD,
GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE,
SN, TD, TG
PRAI US 2003-493713P P 20030807
US 2004-579177P P 20040612
AB The present invention relates to a pigment epithelium derived
factor ('
PEDF') receptor designated ***PEDF*** -R and
PEDF -R
encoding nucleic acid and amino acid sequences of human,
mouse and rat.
Wild type ***PEDF*** -R, ***PEDF*** -R variants, sol.
PEDF
-R variants, chimeric ***PEDF*** -R, and antibodies which bind
to the
PEDF -R (including agonist and neutralizing antibodies),
as well as
various uses for these mols. are described. Assay systems for
detecting
ligands to ***PEDF*** -R, systems for studying the physiol. role
of
PEDF -R and its ligands, diagnostic techniques for
identifying
PEDF -related conditions, therapeutic techniques for the
treatment
of ***PEDF*** -related and ***PEDF*** -R related conditions,
and
methods for identifying mols. homologous to ***PEDF*** -R.
The present
invention further provides an antibody for ***PEDF*** -R and
hybridomas

capable of secreting antibodies. The present invention provides a method of treating a neurol. disease, an ocular disease, angiogenesis disorder or neovascularization in a subject comprising administering to the subject a therapeutically effect amt. of pharmaceutical compn. of the present invention.

L5 ANSWER 5 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:572577 CAPLUS
DN 143:72270
TI Angiostatin, pigment epithelium-derived factor, and SLED compounds useful in inhibiting vascular leakage, inflammation and fibrosis
IN Ma, Jian-Xing
PA USA
SO U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
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PI US 2005143300	A1	20050630	US 2004-963115
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20041012

PRAI US 2003-510620P P 20031010

AB The present invention is directed to a method of inhibiting at least one of vascular leakage, inflammation and fibrosis in an animal by administering to the animal a vascular leakage inhibiting amt. of a

compn., wherein at a substantially higher amt. the compn. is effective in

inhibiting ***angiogenesis***, and wherein the anti-angiogenic

activity of the compn. is sep. from the vascular leakage inhibiting activity of the compn. The animal experiencing at least one of vascular

leakage, inflammation and fibrosis has a disease selected from the group

consisting of diabetes, chronic inflammation, brain edema, arthritis,

uveitis, macular edema, cancer, hyperglycemia, a kidney

inflammatory disease, a disorder resulting in kidney fibrosis, a disorder of the kidney

resulting in proteinuria, and combinations thereof. The compn.

capable of inhibiting at least one of vascular leakage, inflammation and fibrosis is

selected from the group consisting of angiostatin, fragments of angiostatin, analogs or derivs. of angiostatin, pigment epithelium-derived

factor, fragments of pigment epithelium-derived factor, analogs or derivs.

of pigment epithelium-derived factor and combinations thereof.

L5 ANSWER 6 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:999236 CAPLUS

TI Use of recombinant adeno-associated virus vectors encoding antiangiogenic

factor for treating or preventing neovascularization of diseased eyes

IN Manning, William C., Jr.; Dwarki, Varavani J.; Rendahl,

Katherine; Zhou,

Shangzhen; Miller, Sheldon S.; Wang, Fei

PA The Regents of the University of California, USA; Chiron

Corporation

SO U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 525,956,

abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.
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PI US 6943153	B1	20050913	US 2000-665493
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20000920

WO 2002024234 A2 20020328 WO 2001-US29480

20010920

WO 2002024234 A3 20021227

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,

MC, NL,

PT, SE, TR

AU 2001092881 A5 20020402 AU 2001-92881

20010920

US 2002194630 A1 20021219 US 2002-90983

20020304

PRAI US 1999-124460P P 19990315

US 2000-174984P P 20000106

US 2000-525956 B2 20000315

US 2000-665493 A 20000920

WO 2001-US29480 W 20010920

AB The present invention provides a method of ***inhibiting***

angiogenesis in a diseased ***eye*** of a subject,

comprising,

administering intraocularly a recombinant adeno-assocd. virus

(rAAV) gene

delivery vector which directs the expression of an antiangiogenic

factor,

such that administration of said vector ***inhibits***

neovascularization of the diseased ***eye***.

Specifically,

said anti-angiogenic factor is sol. Flt-1, ***PEDF***, sol. Tie-2

receptor, or a single chain anti-VEGF antibody. The diseased

eye

is in a subject having diabetic retinopathy, wet AMD or

retinopathy of

prematurity.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE

FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 100 EMBASE COPYRIGHT (c) 2005 Elsevier

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DUPLICATE 1

AN 2005268935 EMBASE

TI Two functional epitopes of pigment epithelial-derived factor

block

angiogenesis and induce differentiation in prostate

cancer.

AU Filleur S.; Volz K.; Nelius T.; Mirochnik Y.; Huang H.; Zaichuk

T.A.;

Aymerich M.S.; Becerra S.P.; Yap R.; Veliceasa D.; Shroff E.H.;

Volpert

O.V.

CS O.V. Volpert, Department of Urology, Feinberg School of

Medicine,

Northwestern University, 300 East Superior Street, Chicago, IL

60611,

United States. olgavolp@northwestern.edu

SO Cancer Research, (15 Jun 2005) Vol. 65, No. 12, pp. 5144-

5152.

Refs: 57

ISSN: 0008-5472 CODEN: CNREA8

CY United States

DT Journal; Article

FS 016 Cancer

028 Urology and Nephrology

030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 20050707

Last Updated on STN: 20050707

AB Pigment epithelial-derived factor (***PEDF***), an

angiogenesis ***inhibitor*** with neurotrophic

properties,

balances angiogenesis in the ***eye*** and blocks tumor

progression.

Its neurotrophic function and the ability to block vascular leakage

is

replicated by the ***PEDF*** 44-mer peptide (residues 58-

101). We

analyzed PEDFs' three-dimensional structure and identified a

potential

receptor-binding surface. Seeking ***PEDF***-based

antiangiogenic

agents we generated and tested peptides representing the

middle and lower

regions of this surface. We identified previously unknown

antiangiogenic

epitopes consisting of the 34-mer (residues 24-57) and a shorter

proximal

peptide (TGA, residues 16-26) with the critical stretch

L(19)VEEED(24) and

a fragment within the 44-mer (ERT, residues 78-94), which

retained

neurotrophic activity. The 34-mer and TGA, but not the 44-mer

reproduced

PEDF angiogenic signals hinged on c-jun-NH

(2)-kinase-dependent nuclear factor of activated T cell

deactivation and

caused apoptosis. Conversely, the ERT, but not the 34-mer/TGA

induced

neuronal differentiation. For the 44-mer/ERT, we showed a

novel ability

to cause neuroendocrine differentiation in prostate cancer cells.

PEDF and the peptides bound endothelial and PC-3 prostate cancer cells. Bound peptides were displaced by ***PEDF***, but not by each other, suggesting multiple receptors. ***PEDF*** and its active fragments blocked tumor formation when conditionally expressed by PC-3 cells. The 34- and 44-mer used distinct mechanisms: the 34-mer acted on endothelial cells, ***blocked*** ***angiogenesis***, and induced apoptosis whereas 44-mer prompted neuroendocrine differentiation in cancer cells. Our results map active regions for the two ***PEDF*** functions, signaling via distinct receptors, identify candidate peptides, and provide their mechanism of action for future development of ***PEDF***-based tumor therapies. .COPYRG.T. 2005 American Association for Cancer Research.

L5 ANSWER 8 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:318192 CAPLUS
DN 142:476326
TI The neuroprotective and ***angiogenesis*** ***inhibitory*** serpin, ***PEDF*** : New insights into phylogeny, function, and signaling
AU Tombran-Tink, Joyce
CS Division of Pharmaceutical Sciences, University of Missouri-Kansas City, Kansas City, MO, 64110, USA
SO Frontiers in Bioscience (2005), 10(Suppl.), 2131-2149
CODEN: FRBIF6; ISSN: 1093-4715
URL:
<http://www.bioscience.org/asp/getfile.asp?FileName=/2005/v10/at/1686/1686.pdf>
PB Frontiers in Bioscience
DT Journal; General Review; (online computer file)
LA English
AB A review. Pigment Epithelial-Derived Factor (***PEDF***) is a non-inhibitory serpin with neuroprotective and antiangiogenic actions. It is a potent and broadly acting neurotrophic factor that protects neurons from many regions of the central nervous system against a wide range of neurodegenerative insults including glutamate toxicity and oxidative stress. ***PEDF*** also functions as a natural ***inhibitor*** of ***angiogenesis***, targeting the growth of only new vessels. The 50-kDa protein is encoded by a single gene that shows strong conservation across phyla from fish to mammals. Two specific domains on the ***PEDF*** protein interact with extracellular matrix components and may mediate some of the biol. actions of this protein. The transducers through which ***PEDF*** signals neurons and endothelial cells are defined and involves major pathways including Akt/NFkB, MAPK, and the caspases. ***PEDF*** is widely expressed in the nervous system and in most tissues of the body. A significant amt. of the protein is found in the cerebrospinal fluid and circulating plasma as well. Therapeutic administration of the sol. protein or viral-mediated transfer of the gene in exptl. in vivo models suggests that ***PEDF*** is an excellent pharmacol. tool for slowing the progression of a range of neurodegenerative diseases and those pathologies assoc. with abnormal vessel growth in the ***eye*** and metastatic cancers of various tissues.

RE.CNT 107 THERE ARE 107 CITED REFERENCES
AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 100 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
DUPLICATE 2
AN 2005167594 EMBASE
TI Met72Thr polymorphism of pigment epithelium-derived factor gene and susceptibility to age-related macular degeneration.

AU Yamagishi S.; Nakamura K.; Inoue H.; Takeuchi M.
CS S. Yamagishi, Department of Medicine, Kurume University, School of Medicine, 67 Asahi-machi, Kurume 830-0011, Japan.
shoichi@med.kurume-u.ac.jp
SO Medical Hypotheses, (2005) Vol. 64, No. 6, pp. 1202-1204.
Refs: 16
ISSN: 0306-9877 CODEN: MEHYDY
CY United Kingdom
DT Journal; (Short Survey)
FS 012 Ophthalmology
022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20050526
Last Updated on STN: 20050526
AB Age-related macular degeneration (ARMD) is the most common cause of acquired blindness among the people of occupational age. Although the pathogenesis of ARMD is not fully understood, several studies suggest a possible contribution of a genetic factor in the development and progression of ARMD. Pigment epithelium-derived factor (***PEDF***), a glycoprotein that belongs to the superfamily of serine protease inhibitors, was first purified from the conditioned media of human retinal pigment epithelial cells as a factor with potent neuronal differentiating activity in human retinoblastoma cells. Recently, ***PEDF*** has been shown to be a highly effective ***inhibitor*** of ***angiogenesis*** in cell culture and animal models. In addition, ***PEDF*** has been found in the vitreous, and its levels were decreased in angiogenic ***eye*** diseases, thus suggesting that a loss of ***PEDF*** in the ***eye*** is functionally important in the pathogenesis of ARMD. A functional amino acid change, a methionine to threonine polymorphism (Met72Thr polymorphism) at codon 72 in exon 3 (T/C polymorphism) of the ***PEDF*** gene, that results in the formation of BstSI restriction site, has recently been identified. Since it is well known that a single nucleotide polymorphism and resultant amino acid change often alters the activity or expression level of the target protein, we would like to propose here a novel hypothesis that the Met72Thr polymorphism (T/C polymorphism) of ***PEDF*** gene may be a genetic marker for ARMD. Are genotype and allele frequencies of the Met72Thr polymorphism (T/C polymorphism) different between the patients with or without ARMD? Is this polymorphism associated with disease severity and progression? If the answer is yes, does this Met72Thr polymorphism regulate the vitreous levels of ***PEDF*** ? These clinical studies could provide us with information whether this genetic variant of the ***PEDF*** gene could present an attractive candidate susceptibility gene for ARMD. .COPYRG.T. 2005 Elsevier Ltd. All rights reserved.

L5 ANSWER 10 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:53535 CAPLUS
DN 142:212706
TI Extracellular phosphorylation converts pigment epithelium-derived factor from a neurotrophic to an antiangiogenic factor
AU Maik-Rachline, Galia; Shalitel, Shmuel; Seger, Rony
CS Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel
SO Blood (2005), 105(2), 670-678
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB The pigment epithelium-derived factor (***PEDF***) belongs to the

superfamily of serine protease inhibitors (serpin). There have been 2 distinct functions attributed to this factor, which can act either as a

neurotrophic or as an antiangiogenic factor. Besides its localization in the ***eye***, ***PEDF*** was recently reported to be present also in human plasma. We found that ***PEDF*** purified from plasma is a phosphoprotein, which is extracellularly phosphorylated by protein kinase CK2 (CK2) and to a lesser degree, intracellularly, by protein kinase A (PKA). CK2 phosphorylates ***PEDF*** on 2 main residues, Ser24 and Ser114, and PKA phosphorylates ***PEDF*** on one residue only, Ser227.

The physiol. relevance of these phosphorylations was detd. using phosphorylation site mutants. We found that both CK2 and PKA phosphorylations of ***PEDF*** markedly affect its physiol. function.

The fully CK2 phosphorylation site mutant S24, 114E abolished ***PEDF*** neurotrophic activity but enhanced its antiangiogenic activity, while the PKA phosphorylation site mutant S227E reduced ***PEDF*** antiangiogenic activity. This is a novel role of extracellular phosphorylation that is shown here to completely change the nature of

PEDF from a neurotrophic to an antiangiogenic factor. RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

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DUPLICATE 3

AN 2005213775 EMBASE

TI Pericocular gene transfer of pigment epithelium-derived factor ***inhibits*** choroidal ***neovascularization*** in a human-sized ***eye***

AU Saishin Y.; Silva R.L.; Saishin Y.; Kachi S.; Aslam S.; Yuan Y.G.; Lai H.; Carrion M.; Harris B.; Hamilton M.; Wei L.; Campochiaro P.A.

CS Dr. P.A. Campochiaro, Maumenee 719, Johns Hopkins University, School of Medicine, 600 N. Wolfe Street, Baltimore, MD 21287-9277, United States. pcampo@jhmi.edu

SO Human Gene Therapy, (2005) Vol. 16, No. 4, pp. 473-478. Refs: 17

ISSN: 1043-0342 CODEN: HGTHE3

CY United States

DT Journal; Article

FS 012 Ophthalmology

022 Human Genetics

037 Drug Literature Index

LA English

SL English

ED Entered STN: 20050602

Last Updated on STN: 20050602

AB Gene transfer provides a potential way to achieve sustained delivery of therapeutic proteins to the ***eye***. Studies in rodents have suggested that pericocular injection of adenoviral vectors containing

expression cassettes for antiangiogenic proteins results in high intraocular levels of the proteins and ***suppression*** of choroidal

neovascularization (CNV). However, the differences in size and scleral thickness between mouse and human eyes make it difficult to

ascertain if pericocular gene transfer is a feasible approach for treating human choroidal diseases. To address this issue, we tested the effect of

pericocular injection of an expression cassette for pigment epithelium-derived factor (***PEDF***) packaged in adenoviral vector

(AdPEDF.11) in a CNV model in pigs, which have eyes that are very similar

to humans in size and scleral thickness. Pericocular injection of .beta.-galactosidase (AdLacZ.11) resulted in prominent transduction of

pericocular tissues, as was seen in mice. Pericocular injection of AdPEDF.11 caused increased levels of ***PEDF*** in the choroid and

significantly reduced the amount of CNV at rupture sites in Bruch's

membrane. These data suggest that pericocular gene transfer may be feasible for treatment of human choroidal diseases. .COPYRG. Mary Ann Liebert, Inc.

L5 ANSWER 12 OF 100 EMBASE COPYRIGHT (c) 2005

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DUPLICATE 4

AN 2004480206 EMBASE

TI How ***PEDF*** prevents angiogenesis: A hypothesized pathway.

AU Ren J.-G.; Jie C.; Talbot C.

CS jgren@rics.bwh.harvard.edu

SO Medical Hypotheses, (2005) Vol. 64, No. 1, pp. 74-78.

Refs: 35

ISSN: 0306-9877 CODEN: MEHYDY

PUI S 0306-9877(04)00391-3

CY United Kingdom

DT Journal; General Review

FS 030 Pharmacology

LA English

SL English

ED Entered STN: 20041202

Last Updated on STN: 20041202

AB Pigment epithelium-derived factor (***PEDF***) is a multiple functional protein, coded by the serine proteinase inhibitor, clade F,

member 1 (SERPINF1) gene, which has both anti-angiogenic activity and neurotrophic activity at the same time. Its antiangiogenic activity in

the mammalian ***eye*** is the most potent known at this time. However, the mechanism(s) by which ***PEDF*** works in vivo is still

uncertain. Some observations suggest that ***PEDF*** can simultaneously inhibit the migration and proliferation induced by vascular

endothelial growth factor (VEGF), and then further ***inhibits***

angiogenesis by interacting with specific cell surface

receptors, but no such receptor has been reported to date. Here we

propose a hypothesis that ***PEDF*** exerts its function by binding with

integrins. Integrin can therefore serve as the receptor of

PEDF

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L5 ANSWER 13 OF 100 EMBASE COPYRIGHT (c) 2005

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DUPLICATE 5

AN 2005139428 EMBASE

TI Pigment epithelium-derived factor inhibits oxidative stress-induced

apoptosis and dysfunction of cultured retinal pericytes.

AU Amano S.; Yamagishi S.-I.; Inagaki Y.; Nakamura K.; Takeuchi M.; Inoue H.;

Imaizumi T.

CS S.-I. Yamagishi, Department of Internal Medicine III, Kurume University, School of Medicine, 67 Asahi-Machi, Kurume 830-0011, Japan.

shoichi@med.kurume-u.ac.jp

SO Microvascular Research, (2005) Vol. 69, No. 1-2, pp. 45-55.

Refs: 52

ISSN: 0026-2862 CODEN: MIVRA6

CY United States

DT Journal; Article

FS 012 Ophthalmology

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 20050428

Last Updated on STN: 20050428

AB Pigment epithelium-derived factor (***PEDF***) is a potent

inhibitor of ***angiogenesis*** in the mammalian

eye

, suggesting that loss of ***PEDF*** is implicated in the

pathogenesis of proliferative diabetic retinopathy. However, a role for

PEDF in early diabetic retinopathy remains to be elucidated. Since

oxidative stress is thought to be involved in pericyte loss and dysfunction,

one of the changes characteristic of early diabetic retinopathy, we

investigated whether and how ***PEDF*** could protect cultured retinal

pericyte against oxidative stress injury. High glucose (30 mM) increased

intracellular reactive oxygen species (ROS) generation in

pericytes, which was completely blocked by ***PEDF***. High glucose or

H(2)O(2) was

found to induce growth retardation and apoptotic cell death of pericytes. ***PEDF*** completely restored these cytopathic effects on pericytes. An increased ratio of bax to bcl-2 mRNA level with subsequent activation of caspase-3 was observed in high-glucose- or H(2)O(2)-exposed pericytes, which was also completely prevented by ***PEDF***. ***PEDF*** significantly increased glutathione peroxidase (GPx) mRNA levels and activity in pericytes. Further, ***PEDF*** was found to completely inhibit high-glucose- or H(2)O(2)-induced increase in a mRNA ratio of angiotensin-2 to angiotensin-1 and up-regulation of VEGF mRNA levels in pericytes. ***PEDF*** mRNA levels themselves were down-regulated in high-glucose- or H(2)O(2)-exposed pericytes. These results demonstrate that ***PEDF*** protects against high-glucose- or H(2)O(2)-induced pericyte apoptosis and dysfunction through its anti-oxidative properties via GPx induction. Our present study suggests that substitution of ***PEDF*** proteins might be a promising therapeutic strategy for treatment of patients with early diabetic retinopathy. .COPYRG.T. 2004 Elsevier Inc. All rights reserved.

L5 ANSWER 14 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:45589 CAPLUS
DN 142:258393
TI Vitamin A up-regulates the expression of thrombospondin-1 and pigment epithelium-derived factor in retinal pigment epithelial cells
AU Uchida, Hiroko; Hayashi, Hideyuki; Kuroki, Motomu; Uno, Koichi; Yamada, Hiromi; Yamashita, Yuichi; Tombran-Tink, J.; Kuroki, Masahide; Oshima, Kenji
CS Department of Ophthalmology, School of Medicine, Fukuoka University, Fukuoka, 814-0180, Japan
SO Experimental Eye Research (2005), 80(1), 23-30
CODEN: EXERA6; ISSN: 0014-4835
PB Elsevier
DT Journal
LA English
AB Vitamin A is essential for the visual system. It is metabolized in the retina and the resulting product, retinoic acid (RA), greatly affects the structure and functions of retinal pigment epithelial (RPE) cells. RPE cells produce a variety of extracellular matrix (ECM) proteins and angiogenic factors, both of which are expressed at varying levels in the normal RPE layer. In this study, we investigated the effect of all-trans-retinoic acid on the prodn. of an ECM protein, thrombospondin-1 (TSP-1), and two angiogenic factors, pigment epithelium-derived factor (***PEDF***) and vascular endothelial growth factor (VEGF) by RPE cells. RA increased the release of TSP-1 and ***PEDF***, but not that of VEGF, from human RPE cells in vitro. In vitamin A-deficient mice, the expression of TSP-1 and ***PEDF*** in the RPE layer considerably decreased compared with that of normal control mice. The vitamin A deficiency hardly affected the accumulation of VEGF in the RPE layer. These findings suggest that vitamin A modulates the structure and anti-angiogenic functions of the RPE layer partly by up-regulating the expression of the angiogenesis-related ECM protein, TSP-1, and the anti-angiogenic factor, ***PEDF***.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:333513 CAPLUS
DN 143:113591
TI Immunological Factors in the Pathogenesis and Treatment of Age-Related Macular Degeneration
AU Kijstra, A.; La Heij, E.; Hendrikse, F.
CS Eye Research Institute Maastricht, Department of Ophthalmology, University of Maastricht, Maastricht, Neth.
SO Ocular Immunology and Inflammation (2005), 13(1), 3-11
CODEN: OIINEN; ISSN: 0927-3948
PB Taylor & Francis Inc.
DT Journal; General Review
LA English
AB A review. Recent findings indicate that immunol. factors are involved not only in the pathogenesis of age-related macular degeneration (AMD), but also in its treatment. Earlier data showing the presence of inflammatory cells in affected areas of AMD retinas support this statement. Although a possible role for autoimmunity was initially suggested, it has never reached general acceptance. Microorganisms have also been implicated in the pathogenesis of AMD. Both serum antibacterial antibody levels and pos. DNA tests from neovascular membranes have pointed to a possible role for Chlamydia pneumoniae in the pathogenesis of AMD. New data is providing evidence for the hypothesis that deposits between Bruch's membrane and the retinal pigment epithelium (RPE) cell layer may act as a stimulus for the local activation of the complement system. This may lead to a further growth of the deposits due to the strong chemotactic activity of certain complement activation products (such as C5a) with an influx of inflammatory cells. The buildup of cells and extracellular deposits may lead to local ischemia resulting in the activation of RPE cells. These activated RPE cells are thought to release angiogenic stimuli leading to choroidal neovascularization, which is the most serious complication of AMD. The fact that immunosuppressive drugs such as triamcinolone acetonide and anecortave acetate are capable of ***inhibiting*** choroidal ***neovascularization*** is consistent with an inflammatory component in the pathogenesis of AMD. Specific immunotherapy directed at certain cytokines or growth factors is now being investigated at both the animal and patient levels. Various clin. trials involving engineered antibodies are now being applied to ***block*** ***angiogenic*** factors such as the vascular endothelial growth factor (VEGF). An approach using gene therapy to influence angiogenesis by inducing the prodn. of the pigment epithelium-derived factor (***PEDF***) was able to ***block*** ***neovascularization*** in an exptl. murine model. Besides trying to block ongoing processes in AMD, retinal transplantation is now also being investigated as a treatment option. The fact that the retina is possibly an immunoprivileged tissue in combination with exptl. data showing that the subretinal space is an immunoprivileged site is an indication that transplantation would not suffer from the rejection process. A larger obstacle is the question whether transplanted retinal tissue will regain its functional properties.
RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 100 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:415605 BIOSIS
DN PREV200400419260
TI Methods and compositions for ***inhibiting*** ***angiogenesis***
DUPLICATE 6

AU Bouck, Noel P. [Inventor, Reprint Author]; Dawson, David W. [Inventor];
Gillis, Paul R. [Inventor]; Volpert, Olga [Inventor]; Crawford, Susan E.

[Inventor]; Stellmach, Veronica M. [Inventor]

CS Occidental, CA, USA

ASSIGNEE: Northwestern University

PI US 6797691 20040928

SO Official Gazette of the United States Patent and Trademark

Office Patents,

(Sep 28 2004) Vol. 1286, No. 4.

http://www.uspto.gov/web/menu/patdata.html

. e-file.

ISSN: 0098-1133 (ISSN print).

DT Patent

LA English

ED Entered STN: 27 Oct 2004

Last Updated on STN: 27 Oct 2004

AB The present invention provides a method of ***inhibiting***

angiogenesis within a tissue by providing exogenous

PEDF

to cells associated with the tissue. The presence of exogenous

PEDF ***inhibits*** ***angiogenesis*** within the

tissue,

in part by interfering with the ability of vascular endothelia to

expand

within the tissue. The invention also provides a method for

determining

the severity of a tumor by assaying for the presence of

PEDF

within the tumor. The invention further provides a method of

inhibiting

endothelial cell migration, a method of stimulating the growth of

hair in

a mammal, a method for inhibiting the growth of a tumor, a

method of

inducing differentiation of a neuroblastoma cell, a method of

slowing the

growth of a neuroblastoma cell, and method of treating ischemic

retinopathy in a mammal. To facilitate the inventive methods, the

present

invention provides pharmaceutical compositions including

sources of

PEDF

L5 ANSWER 17 OF 100 CAPLUS COPYRIGHT 2005 ACS on

STN

AN 2004:291961 CAPLUS

DN 140:298102

TI Anti-angiogenic fragments of pigment epithelium-derived factor (

PEDF)

IN Volz, Karl; Fileur, Stephanie; Volpert, Olga V.; Zaichuk, Tetiana

PA The Board of Trustees of the University of Illinois, USA;

Northwestern

University

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO.

DATE

PI WO 2004028559 A1 20040408 WO 2003-US30264

20030926

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,

CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,

LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,

SY, TJ, TM,

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,

AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,

DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,

SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

PRAI US 2002-413685P P 20020926

US 2002-417688P P 20021010

AB The present invention provides anti-angiogenic derived from

pigment

epithelium-derived factor (***PEDF***) pharmaceutical

compos.

comprising the peptides, and methods of preventing

angiogenesis. Such

methods are useful in treating angiogenesis-assocd. disorders

and

diseases. Also claimed is a method of predicting whether a

diabetic

patient will develop proliferative retinopathy comprising detg. the

ratio

of vascular endothelial growth factor (VEGF) to ***PEDF*** in

an

ocular fluid sample from said patient.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE

FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 100 CAPLUS COPYRIGHT 2005 ACS on

STN

AN 2004:681181 CAPLUS

DN 141:212730

TI Polymer modified anti-angiogenic serpins with extended half-life

for

inhibition of ***angiogenic*** diseases

IN Kumar, Sanjeev

PA USA

SO U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO.

DATE

PI US 2004161423 A1 20040819 US 2003-619149

20030714

PRAI US 2002-396786P P 20020718

AB What is provided is a method of improving the

angiogenesis -

inhibitory effect of an antiangiogenic serpin, or

antiangiogenic

fragment thereof, by covalently linking a polymer moiety to the

serpin

such that the biol. half-life of the serpin is extended. The method

provides for inhibition of diseases having a pathol. angiogenic

component

by administering in vivo an antiangiogenic serpin, or fragment

thereof,

having a covalently linked polymer moiety. Diseases

characterized by

pathol. angiogenesis include diabetic retinopathy, age-related

macular

degeneration, rheumatoid arthritis, endometriosis, psoriasis,

juvenile

hemangioma, and cancer. In one embodiment, the

antiangiogenic serpin is

selected from the group: ***PEDF***, maspin, antithrombin III,

angiotensinogen and headpin. The present inventors undertook

to improve

the biol. activity of the antiangiogenic serpins by polymer

modification

and are the first to disclose use of PEGylated antiangiogenic

serpins for

use in improving the antitumor effects of these proteins. In one

embodiment, ***PEDF*** protein was PEGylated using

tresylated

monomethoxypolyethylene glycol (TMPEG). The 1 .mu.g dose

of PEGylated

PEDF resulted in an improved inhibition of tumor growth

as

compared with unPEGylated ***PEDF***. Unlike tumors in

untreated

animals, which attained a domed appearance, tumors in the

PEGylated

PEDF treated animals were conspicuous for a visible

redn. in

vasculature at all time points and a flatter overall appearance.

This is

consistent with an antiangiogenic effect.

L5 ANSWER 19 OF 100 CAPLUS COPYRIGHT 2005 ACS on

STN

AN 2004:3717 CAPLUS

DN 140:56055

TI Transgenic knockout animal model null for pigment epithelium-

derived

factor (***PEDF***)

IN Bouck, Noel P.; Crawford, Susan E.; Stellmach, Veronica

PA Northwestern University, USA

SO U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO.

DATE

PI US 2004003423 A1 20040101 US 2003-361516
 20030210
 PRAI US 2002-355222P P 20020208
 AB The present invention relates to transgenic knockout animal models null for pigment epithelium-derived factor (***PEDF***). The present invention also provides methods for generating animal disease models and screening methods for identifying biol. active compds. Mice were engineered to be null for ***PEDF*** using SV129 ES cells injected into C57B16 blastocysts. A null allele construct disrupted the ***PEDF*** gene with an IRES-LacZ-Neo cassette between a 4.9 kb 5'-arm and a 3.7 kb 3'-arm. Chimeric animals were obtained and a male chimeric mouse was mated to C57B16 females to obtain mice heterozygous for the ***PEDF*** null allele. Mice heterozygous for the null allele were mated to generate mice homozygous for the null allele of ***PEDF***. The null mice are viable and fertile. The null animals showed abnormalities in multiple systems including the prostate, neural retina, kidney vasculature, and cerebellar granule cells.

L5 ANSWER 20 OF 100 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:537797 CAPLUS
 DN 141:219295
 TI Angiogenesis-related factors derived from retinal glial (Mueller) cells in hypoxia
 AU Eichler, Wolfram; Yafai, Yousef; Wiedemann, Peter; Reichenbach, Andreas
 CS Eye Hospital, University of Leipzig, Leipzig, D-04103, Germany
 SO NeuroReport (2004), 15(10), 1633-1637
 CODEN: NERPEZ; ISSN: 0959-4965
 PB Lippincott Williams & Wilkins
 DT Journal
 LA English
 AB Retinal glial (Mueller) cells may play a major role in vascular ***eye*** diseases as they secrete vascular endothelial growth factor (VEGF), a hypoxia-induced angiogenic cytokine. They also release significant amts. of the anti-angiogenic factors, transforming growth factor (TGF)-beta.2, pigment epithelium derived factor (***PEDF***), and thrombospondin-1 (TSP-1). Exposure of human (MIO-M1) and guinea-pig Mueller cells to hypoxia resulted in a decreased release of TGF-beta.2 and ***PEDF*** but in an elevated secretion of TSP-1. When retinal endothelial cells were exposed to VEGF/anti-angiogenic factor ratios mimicking those found in culture media of Mueller cells under normoxia or hypoxia, their proliferation was significantly inhibited by TGF-beta.2, ***PEDF*** or TSP-1. Thus Mueller cells may provide a permanent anti-proliferative condition for retinal endothelial cells.
 RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l4 and py<=1998
 L6 1 L4 AND PY<=1998

=> d bib abs

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:241907 CAPLUS
 DN 138:251121
 TI Retinal cell lines with extended life-span and their applications
 IN Greenwood, John; Adamson, Peter; Lund, Raymond
 PA Neurotech SA, UK
 SO U.S. Pat. Appl. Publ., 55 pp., Cont.-in-part of U.S. 6,090,624.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.
PI US 2003059868	A1	20030327	US 2000-559707

20000427

US 6878544 B2 20050412
 FR 2747690 A1 19971024 FR 1996-4964
 19960419 <--
 FR 2747690 B1 19980612
 WO 9740139 A1 19971030 WO 1997-FR709
 19970418 <--
 W: AU, CA, JP, NZ, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 US 6183735 B1 20010206 US 1998-973553
 19980122
 US 6090624 A 20000718 US 1998-182516
 19981030
 CA 2407424 AA 20011101 CA 2001-2407424
 20010427
 WO 2001081551 A2 20011101 WO 2001-IB860
 20010427
 WO 2001081551 A3 20021017
 WO 2001081551 C1 20030103
 WO 2001081551 C2 20020815
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1287115 A2 20030305 EP 2001-931995
 20010427
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003530880 T2 20031021 JP 2001-578622
 20010427
 PRAI FR 1996-4964 A 19960419
 WO 1997-FR709 W 19970418
 US 1998-973553 A2 19980122
 US 1998-182516 A2 19981030
 US 2000-559707 A 20000427
 WO 2001-IB860 W 20010427
 AB The invention features retina-derived (retinal endothelial or retinal epithelial pigment) cell lines with extended life-span and capable of being implanted in the retina and of carrying a therapeutic substance to the ***eye*** and to the central nervous system. Such lines can also be used as a model for studying blood/central nervous system interfaces. These lines are derived from primary retinal cultures selected from the group consisting of primary retinal endothelial cells and primary retinal epithelial cells, comprise a polynucleotide contg. an oncogene, which polynucleotide is optionally assocd. with at least one selection gene, and have the morphol. characteristics and at least the expression characteristics of the surface antigens of corresponding primary cultures.

=> d his

(FILE 'HOME' ENTERED AT 16:46:45 ON 27 SEP 2005)

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 16:47:01 ON 27 SEP 2005
 L1 727 S PEDF
 L2 24387 S (NEOVASCULAR? OR ANGIOGEN?) (3A)
 (INHIBIT? OR SUPPRES? OR BLO
 L3 260 S L1 AND L2
 L4 160 S L3 AND EYE
 L5 100 DUP REM L4 (60 DUPLICATES REMOVED)
 L6 1 S L4 AND PY<=1998

=> s Bouck, N?
 TERM 'N?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
 1 FILES SEARCHED...
 You have entered a truncated stem which occurs in too many terms. Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for

'degradation', you could replace it with the expression 'degrdn OR degrad?'). If your search term was numeric, e.g., 'C>5', reduce the size of the range.

=> s Bouck, N7/au
L7 313 BOUCK, N7/AU

=> s l7 and PEDF
L8 30 L7 AND PEDF

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 13 DUP REM L8 (17 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 13 ANSWERS -
CONTINUE? Y(N):y

L9 ANSWER 1 OF 13 BIOSIS COPYRIGHT (c) 2005 The
Thomson Corporation on STN
DUPLICATE 1
AN 2004:415605 BIOSIS
DN PREV200400419260
TI Methods and compositions for inhibiting angiogenesis.
AU ***Bouck, Noel P.*** [Inventor, Reprint Author]; Dawson,
David W.
[Inventor]; Gillis, Paul R. [Inventor]; Volpert, Olga [Inventor];
Crawford, Susan E. [Inventor]; Stellmach, Veronica M. [Inventor]
CS Occidental, CA, USA
ASSIGNEE: Northwestern University
PI US 6797691 20040928
SO Official Gazette of the United States Patent and Trademark
Office Patents,
(Sep 28 2004) Vol. 1286, No. 4.
<http://www.uspto.gov/web/menu/patdata.html>
e-file.
ISSN: 0098-1133 (ISSN print).
DT Patent
LA English
ED Entered STN: 27 Oct 2004
Last Updated on STN: 27 Oct 2004
AB The present invention provides a method of inhibiting
angiogenesis within
a tissue by providing exogenous ***PEDF*** to cells
associated with
the tissue. The presence of exogenous ***PEDF*** inhibits
angiogenesis within the tissue, in part by interfering with the
ability of
vascular endothelia to expand within the tissue. The invention
also
provides a method for determining the severity of a tumor by
assaying for
the presence of ***PEDF*** within the tumor. The invention
further
provides a method of inhibiting endothelial cell migration, a
method of
stimulating the growth of hair in a mammal, a method for
inhibiting the
growth of a tumor, a method of inducing differentiation of a
neuroblastoma
cell, a method of slowing the growth of a neuroblastoma cell, and
method
of treating ischemic retinopathy in a mammal. To facilitate the
inventive
methods, the present invention provides pharmaceutical
compositions
including sources of ***PEDF***.

L9 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:3717 CAPLUS
DN 140:56055
TI Transgenic knockout animal model null for pigment epithelium-
derived
factor (***PEDF***)
IN ***Bouck, Noel P.*** ; Crawford, Susan E.; Stellmach,
Veronica
PA Northwestern University, USA
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE

PI US 2004003423 A1 20040101 US 2003-361516
20030210
PRAI US 2002-355222P P 20020208
AB The present invention relates to transgenic knockout animal
models null
for pigment epithelium-derived factor (***PEDF***). The
present

invention also provides methods for generating animal disease
models and
screening methods for identifying biol. active compds. Mice were
engineered to be null for ***PEDF*** using SV129 ES cells
injected
into C57B16 blastocysts. A null allele construct disrupted the
PEDF gene with an IRES-LacZ-Neo cassette between a
4.9 kb 5'-arm
and a 3.7 kb 3'-arm. Chimeric animals were obtained and a male
chimeric
mouse was mated to C57B16 females to obtain mice
heterozygous for the
PEDF null allele. Mice heterozygous for the null allele
were
mated to generate mice homozygous for the null allele of
PEDF.
The null mice are viable and fertile. The null animals showed
abnormalities in multiple systems including the prostate, neural
retina,
kidney vasculature, and cerebellar granule cells.

L9 ANSWER 3 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier
B.V. All rights
reserved on STN
DUPLICATE 2
AN 2003250315 EMBASE
TI Pigment epithelium-derived factor regulates the vasculature and
mass of
the prostate and pancreas.
AU Doll J.A.; Stellmach V.M.; ***Bouck N.P.*** ; Bergh A.R.J.;
Lee C.;
Abramson L.P.; Cornwell M.L.; Pins M.R.; Borensztajn J.;
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SO Nature Medicine, (1 Jun 2003) Vol. 9, No. 6, pp. 774-780.
Refs: 45
ISSN: 1078-8956 CODEN: NAMEFI
CY United States
DT Journal; Article
FS 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 20030710
Last Updated on STN: 20030710
AB Angiogenesis sustains tumor growth and metastasis, and
recent studies
indicate that the vascular endothelium regulates tissue mass. In
the
prostate, androgens drive angiogenic inducers to stimulate
growth, whereas
androgen withdrawal leads to decreased vascular endothelial
growth factor,
vascular regression and epithelial cell apoptosis. Here, we
identify the
angiogenesis inhibitor pigment epithelium-derived factor (***PEDF***)
as a key inhibitor of stromal vasculature and epithelial tissue
growth in
mouse prostate and pancreas. In ***PEDF*** -deficient mice,
stromal
vessels were increased and associated with epithelial cell
hyperplasia.
Androgens inhibited prostatic ***PEDF*** expression in
cultured cells.
In vivo, androgen ablation increased ***PEDF*** in normal rat
prostates and in human cancer biopsies. Exogenous
PEDF induced
tumor epithelial apoptosis in vitro and limited in vivo tumor
xenograft
growth, triggering endothelial apoptosis. Thus, ***PEDF***
regulates
normal pancreas and prostate mass. Its androgen sensitivity
makes
PEDF a likely contributor to the anticancer effects of
androgen
ablation.

L9 ANSWER 4 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier
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DUPLICATE 3
AN 2003187418 EMBASE
TI Low content of the natural ocular anti-angiogenic agent pigment
epithelium-derived factor (***PEDF***) in aqueous humor
predicts
progression of diabetic retinopathy.
AU Boehm B.O.; Lang G.; Volpert O.; Jehte P.M.; Kurkhaus A.;
Rosing S.;

Lang G.K.; ***Bouck N.***
 CS Dr. B.O. Boehm, Div. of Endocrinology and Diabetes,
 Department of Internal
 Medicine, University of Ulm Medical School, Robert-Koch-
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 SO Diabetologia, (1 Mar 2003) Vol. 46, No. 3, pp. 394-400.
 Refs: 39
 ISSN: 0012-186X CODEN: DBTGAJ
 CY Germany
 DT Journal; Article
 FS 003 Endocrinology
 006 Internal Medicine
 012 Ophthalmology
 037 Drug Literature Index
 LA English
 SL English
 ED Entered STN: 20030522
 Last Updated on STN: 20030522
 AB Aims/hypothesis. Retinopathy is the most common
 microvascular
 complication of diabetes. Our aim was to address the predictive
 value of
 pro-angiogenic and anti-angiogenic markers for progression of
 retinopathy.
 Methods. Aqueous humor was collected at cataract surgery from
 32 diabetic
 patients who had no or very mild retinopathy (ETDRS stage
 .ltoreq.20) and
 33 normoglycaemic control subjects. Content of pro-angiogenic
 vascular
 endothelial growth factor and angiogenic inhibitor pigment
 epithelium-derived factor were determined. Angiogenic activity
 was
 quantified by measuring its effect on the migration of capillary
 endothelial cells. The predictive value of the initial level of these
 markers for progression of retinopathy was studied by following
 the
 probands for a maximum of 75 months. Results. In the aqueous
 fluid
 content of vascular endothelial growth factor was increased in
 diabetic
 patients (mean values 492 versus 292 pg/ml; p=0.0052), and
 pigment
 epithelium-derived factor values were decreased (mean values
 1740 versus
 3680 ng/ml; p=0.0058) compared to control subjects. Of the
 diabetic
 patients ten progressed during follow-up (ETDRS stage >47B).
 This
 subgroup showed lower pigment epithelium-derived factor
 content when
 compared to non-progressors and control subjects. Migratory
 activity in
 samples of patients from the control group and in diabetic
 patients
 without progression was generally inhibitory due to pigment
 epithelium-derived factor. Inhibition was blocked by neutralizing
 antibodies to pigment epithelium-derived factor. In diabetic
 patients
 initial angiogenic activity was higher in those who later developed
 retinopathy (vs. controls p=0.00005; vs. no progressors
 p=0.0003). Both
 pigment epithelium-derived factor and migratory response
 predicted
 progression. Conclusion/Interpretation. Pigment epithelium-
 derived
 factor is an important negative regulator of angiogenic activity of
 aqueous humor. Its content in the aqueous humor of diabetic
 patients
 strongly predicts who among them will develop progression of
 retinopathy.

L9 ANSWER 5 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier
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 AN 2003371039 EMBASE
 TI Proliferative diabetic retinopathy is associated with a low level of
 the
 natural ocular anti-angiogenic agent pigment epithelium-derived
 factor (***PEDF***) in aqueous humor. A pilot study.
 AU Boehm B.O.; Lang G.; Feldmann B.; Kurkhaus A.; Rosinger S.;
 Volpert O.;
 Lang G.K.; ***Bouck N.***
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 SO Hormone and Metabolic Research, (1 Jun 2003) Vol. 35, No. 6,
 pp. 382-386.
 Refs: 32

ISSN: 0018-5043 CODEN: HMMRA2
 CY Germany
 DT Journal; Article
 FS 012 Ophthalmology
 029 Clinical Biochemistry
 LA English
 SL English
 ED Entered STN: 20031002
 Last Updated on STN: 20031002
 AB Retinopathy is the most common microvascular diabetes
 complication and
 represents a major threat to the eyesight. The aim of this study
 was to
 address the role of pro- and anti-angiogenic molecules in diabetic
 retinopathy in the aqueous humor of the eye. Aqueous humor
 was collected
 at cataract surgery from 19 diabetic patients and from 13 age-
 and
 sex-matched normoglycemic controls. Levels of pro-angiogenic
 vascular
 endothelial growth factor (VEGF) and angiogenic inhibitor
 pigment
 epithelium-derived factor (***PEDF***) were determined.
 Angiogenic
 activity of the aqueous humor was quantified by measuring its
 effect on
 the migration of capillary endothelial cells. In the aqueous fluid,
 VEGF
 levels were increased in diabetics (mean values: 501 vs. 367
 pg/ml; p =
 0.05), compared to controls. ***PEDF*** was found to be
 decreased in
 diabetics (mean values: 2080 vs. 5780 ng/ml; p = 0.04)
 compared to
 controls. In seven diabetic patients with proliferative retinopathy,
 the
 most profound finding was a significant decrease of the
 PEDF
 level (mean value: 237 ng/ml), whereas VEGF levels were
 comparable to
 diabetic patients without proliferation (mean value: 3153; p =
 0.003).
 Angiogenic activity in samples of patients from the control group
 was
 generally inhibitory due to ***PEDF***, and inhibition was
 blocked by
 neutralizing antibodies to ***PEDF***. Likewise, in diabetics
 without
 proliferation, angiogenic activity was also blocked by antibodies
 to
 PEDF. We will demonstrate here that the level of the
 natural
 ocular anti-angiogenic agent ***PEDF*** is inversely
 associated with
 proliferative retinopathy. ***PEDF*** is an important negative
 regulator of angiogenic activity of aqueous humor. Our data may
 have
 implications for the development of novel regimens for diabetic
 retinopathy.

L9 ANSWER 6 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier
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 AN 2002242087 EMBASE
 TI ***PEDF***: Anti-angiogenic guardian of ocular function.
 AU ***Bouck N.***
 CS N. Bouck, Dept. of Microbiology-Immunology, Robert H. Lurie
 Compreh.
 Cancer Ctr., Northwestern Univ. Medical School, 310 East
 Superior Street,
 Chicago, IL 60611, United States. n-bouck@northwestern.edu
 SO Trends in Molecular Medicine, (2002) Vol. 8, No. 7, pp. 330-
 334.
 Refs: 45
 ISSN: 1471-4914 CODEN: TMMRCY
 PUI S 1471-4914(02)02362-6
 CY United Kingdom
 DT Journal; General Review
 FS 005 General Pathology and Pathological Anatomy
 012 Ophthalmology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LA English
 SL English
 ED Entered STN: 20020725
 Last Updated on STN: 20020725
 AB Sight-threatening eye diseases can be caused and
 exacerbated by the
 aberrant growth of new blood vessels. Recent work indicates
 that this
 neovascularization not only is a response to a rise in the local

concentration of molecules that induce such angiogenesis but also requires a fall in the levels of endogenous molecules that inhibit angiogenesis.

One of the most potent of these endogenous inhibitors is pigment epithelium-derived factor (***PEDF***), which serves as a survival factor for neuronal components of the eye as well as an essential inhibitor of the growth of ocular blood vessels. Its anti-angiogenic activity is selective in that it is effective against newly forming vessels but spares existing ones, and it is reversible. The molecular basis for this delicate control of endothelial cells is beginning to be understood and strategies to test the ability of ***PEDF*** to ameliorate or prevent vessel damage in the eye are developing rapidly.

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AN 2002275412 EMBASE
TI Pigment epithelium-derived factor is deficient in the vitreous of patients with choroidal neovascularization due to age-related macular degeneration.

AU Hekamp N.M.; ***Bouck N.***; Volpert O.
CS Dr. N.M. Hekamp, Barnes Retina Institute, 1600 South Brentwood Blvd, St. Louis, MO 63141, United States. nhekamp@pol.net
SO American Journal of Ophthalmology, (2002) Vol. 134, No. 2, pp. 220-227.
Refs: 26

ISSN: 0002-9394 CODEN: AJOPAA
PUI S 0002-9394(02)01549-0

CY United States
DT Journal; Article
FS 012 Ophthalmology
020 Gerontology and Geriatrics
029 Clinical Biochemistry

LA English
SL English
ED Entered STN: 20020815
Last Updated on STN: 20020815

AB PURPOSE: Pigment epithelium-derived growth factor (***PEDF***) is a potent inhibitor of angiogenesis that is found in the normal eye.

The purpose of this study is to report decreased levels of ***PEDF*** in the vitreous of eyes with choroidal neovascularization (CNV) due to age-related macular degeneration (AMD). DESIGN: Prospective case-control study. METHODS: In a prospective case-control study, undiluted vitreous was collected from nine eyes of nine patients with CNV due to AMD and from an age-matched control group of 12 eyes of 12 patients with retinal disorders not involving neovascularization. Vitreous ***PEDF*** and vascular endothelial growth factor (VEGF) concentrations were determined by Western blot analyses and enzyme-linked immunosorbent assay (ELISA), respectively. Angiogenic activities of the vitreous samples were assessed in vitro using an endothelial cell chemotaxis assay. RESULTS: In vitreous samples from nine eyes with CNV due to AMD the mean \pm SD ***PEDF*** level was 2.8 ng/ μ L \pm 1.3 ng/ μ L. In vitreous samples from 12 age-matched control eyes the mean \pm SD ***PEDF*** level was 16.4 ng/ μ L \pm 7.1 ng/ μ L. The difference between the two groups was statistically significant ($P = .00003$). No significant difference in vitreous VEGF concentration was seen between CNV/AMD samples and control samples ($P = .23$). All CNV/AMD vitreous samples induced endothelial cell migration in vitro. No sample from age-matched non-age-related macular degeneration controls could induce endothelial cell migration, and 11 of 12 were able to block VEGF-induced migration in vitro. This inhibitory activity required active ***PEDF***. CONCLUSION: The vitreous of

patients with CNV due to AMD contained lower levels of ***PEDF*** and lacked the antiangiogenic activity of vitreous from age-matched controls.

This suggests that loss of ***PEDF*** creates a permissive environment for CNV patients with AMD. .COPYRGT. 2002 by Elsevier Science Inc. All rights reserved.

L9 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN AN 2001:636043 CAPLUS
DN 135:205922

TI Methods and compositions for inhibiting angiogenesis using ***PEDF***

(pigment epithelium differentiation factor)

IN ***Bouck, Noel P.***; Dawson, David W.; Gillis, Paul R.; Crawford, Susan E.; Stellmach, Veronica M.; Volpert, Olga

PA Northwestern University, USA
SO PCT Int. Appl., 100 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.
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PI WO 2001062725	A2	20010830	WO 2001-US5915
20010222			
WO 2001062725	A3	20020321	
W: AU, CA, JP			
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR			

US 6797691	B1	20040928	US 2000-603478
20000623			
CA 2401096	AA	20010830	CA 2001-2401096
20010222			

AU 2001039855	A5	20010903	AU 2001-39855
20010222			
EP 1265627	A2	20021218	EP 2001-914469
20010222			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR			
JP 2004516001	T2	20040603	JP 2001-561733
20010222			

PRAI US 2000-511683	A	20000223	
US 2000-603478	A	20000623	
US 1997-899304	B2	19970723	
US 1998-122079	A2	19980723	
WO 1998-US15228	A2	19980723	
WO 2001-US5915	W	20010222	

AB The present invention provides a method of inhibiting angiogenesis within a tissue by providing exogenous ***PEDF*** to cells assoc. with the tissue. The presence of exogenous ***PEDF*** inhibits angiogenesis within the tissue, in part by interfering with the ability of vascular endothelia to expand within the tissue. The invention also provides a method for detg. the severity of a tumor by assaying for the presence of ***PEDF*** within the tumor. The invention further provides a method of inhibiting endothelial cell migration, a method of stimulating the growth of hair in a mammal, a method for inhibiting the growth of a tumor, a method of inducing differentiation of a neuroblastoma cell, a method of slowing the growth of a neuroblastoma cell, and method of treating ischemic retinopathy in a mammal. To facilitate the inventive methods, the present invention provides pharmaceutical compns. including sources of ***PEDF***.

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AN 2002035104 EMBASE

TI Pigment epithelium-derived factor (***PEDF***) in neuroblastoma: A

multifunctional mediator of Schwann cell antitumor activity.

AU Crawford S.E.; Stellmach V.; Ranalli M.; Huang X.; Huang L.; Volpert O.;

De Vries G.H.; Abramson L.P.; ***Bouck N.***

CS S.E. Crawford, Department of Pathology, R. H. Lurie Comprehensive Cancer

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 SO Journal of Cell Science, (2001) Vol. 114, No. 24, pp. 4421-4428.
 Refs: 58
 ISSN: 0021-9533 CODEN: JNCSAI
 CY United Kingdom
 DT Journal; Article
 FS 008 Neurology and Neurosurgery
 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 ED Entered STN: 20020207
 Last Updated on STN: 20020207
 AB Neuroblastoma is notable for its cellular heterogeneity and unpredictable outcome. Tumors are a variable mixture of primitive malignant neuroblasts, more differentiated ganglionic cells, Schwann and endothelial cells. Although often fatal, neuroblastomas can spontaneously regress, possibly due to favorable autocrine and paracrine interactions among these cells. Here, pigment epithelium-derived factor (***PEDF***), a potent inhibitor of angiogenesis and inducer of neural differentiation, is shown to be produced by ganglionic cells and Schwann cells, but not by more primitive tumor cells. Although undifferentiated neuroblastoma tumor cell secretions were angiogenic primarily due to vascular endothelial growth factor, secretions of Schwann cells were anti-angiogenic due to ***PEDF***. In addition, ***PEDF*** was the major factor responsible for Schwann cell's ability to induce tumor cell differentiation in vitro and recombinant ***PEDF*** had the same effect in vitro and in vivo. Both the growth and the survival of Schwann cells were enhanced by ***PEDF***. Thus ***PEDF*** may serve as a multifunctional antitumor agent in neuroblastomas, inhibiting angiogenesis while promoting the numbers of Schwann cells and differentiated tumor cells that in turn produce ***PEDF***, suggesting that its clinical administration could stimulate a multifaceted antitumor feedback loop with the potential to limit and possibly regress tumor growth.

L9 ANSWER 10 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 8
 AN 2001099898 EMBASE
 TI Prevention of ischemia-induced retinopathy by the natural ocular antiangiogenic agent pigment epithelium-derived factor.
 AU Stellmach V.; Crawford S.E.; Zhou W.; ***Bouck N.***
 CS N. Bouck, Dept. of Microbiology-Immunology, Robert H. Lurie Comprehensive Cancer Ctr., Northwestern University Medical Sch., 320 East Superior Street, Chicago, IL 60611, United States. n-bouck@nwu.edu
 SO Proceedings of the National Academy of Sciences of the United States of America, (27 Feb 2001) Vol. 98, No. 5, pp. 2593-2597.
 Refs: 51
 ISSN: 0027-8424 CODEN: PNASAF
 CY United States
 DT Journal; Article
 FS 005 General Pathology and Pathological Anatomy
 012 Ophthalmology
 LA English
 SL English
 ED Entered STN: 20010412
 Last Updated on STN: 20010412
 AB Aberrant blood vessel growth in the retina that underlies the pathology of proliferative diabetic retinopathy and retinopathy of prematurity is the result of the ischemia-driven disruption of the normally antiangiogenic environment of the retina. In this study, we show that a potent inhibitor of angiogenesis found naturally in the normal eye, pigment epithelium-derived growth factor (***PEDF***), inhibits such aberrant blood vessel growth in a murine model of ischemia-induced retinopathy.

Inhibition was proportional to dose and systemic delivery of recombinant protein at daily doses as low as 2.2 mg/kg could prevent aberrant endothelial cells from crossing the inner limiting membrane. ***PEDF*** appeared to inhibit angiogenesis by causing apoptosis of activated endothelial cells, because it induced apoptosis in cultured endothelial cells and an 8-fold increase in apoptotic endothelial cells could be detected in situ when the ischemic retinas of ***PEDF***-treated animals were compared with vehicle-treated controls. The ability of low doses of ***PEDF*** to curtail aberrant growth of ocular endothelial cells without overt harm to retinal morphology suggests that this natural protein may be beneficial in the treatment of a variety of retinal vasculopathies.

L9 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 AN 2001:287260 BIOSIS
 DN PREV200100287260
 TI The role of ***PEDF*** in the angiostatic effect of penetrating ocular injury.
 AU Penn, J. S. [Reprint author]; Rajaratnam, V. S. [Reprint author]; Koepke, K. A. [Reprint author]; Helton, J. D. [Reprint author]; McGinnis, J. F.;
 Bouck, N. P.
 CS Ophthalmology and Visual Sciences, Vanderbilt Univ School of Med, Nashville, TN, USA
 SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S92. print.
 Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 13 Jun 2001
 Last Updated on STN: 19 Feb 2002

L9 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 AN 2001:287261 BIOSIS
 DN PREV200100287261
 TI Pigment epithelium-derived factor (***PEDF***) inhibits vascular endothelial growth factor (VEGF): Induced retinal permeability and blood flow in vivo.
 AU Clermont, A. C. [Reprint author]; Cahill, M. T. [Reprint author]; Bursell, S.-E. [Reprint author]; ***Bouck, N.***; Aiello, L. P. [Reprint author]
 CS Joslin Diabetes Center, Beetham Eye Institute, Boston, MA, USA
 SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S92. print.
 Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 13 Jun 2001
 Last Updated on STN: 19 Feb 2002

L9 ANSWER 13 OF 13 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 9
 AN 1999247607 EMBASE
 TI Pigment epithelium-derived factor: A potent inhibitor of angiogenesis.
 AU Dawson D.W.; Volpert O.V.; Gillis P.; Crawford S.E.; Xu H.-J.; Benedict W.; ***Bouck N.P.***
 CS N.P. Bouck, Dept. of Microbiology-Immunology, R. H. Lurie Comprehensive Cancer Ctr., Northwestern Univ. Medical School, Chicago, IL 60611, United States. n-bouck@nwu.edu
 SO Science, (9 Jul 1999) Vol. 285, No. 5425, pp. 245-248.
 ISSN: 0036-8075 CODEN: SCIEAS
 CY United States

DT Journal; Article
 FS 005 General Pathology and Pathological Anatomy
 012 Ophthalmology
 LA English
 SL English
 ED Entered STN: 19990802
 Last Updated on STN: 19990802
 AB In the absence of disease, the vasculature of the mammalian eye is quiescent, in part because of the action of angiogenic inhibitors that prevent vessels from invading the cornea and vitreous. Here, an inhibitor responsible for the avascularity of these ocular compartments is identified as pigment epithelium-derived factor (***PEDF***), a protein previously shown to have neurotrophic activity. The amount of inhibitory ***PEDF*** produced by retinal cells was positively correlated with oxygen concentrations, suggesting that its loss plays a permissive role in ischemia-driven retinal neovascularization. These results suggest that ***PEDF*** may be of therapeutic use, especially in retinopathies where pathological neovascularization compromises vision and leads to blindness.

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